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Powell, Goldstein, Frazer & Murphy
P.O. BOX 97223
Washington, DC 20090

EXAMINER
JOHANNSEN, DIANA B

ART UNIT	PAPER NUMBER
1634	

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13

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/697,123	LEE ET AL.	
	Examiner	Art Unit	
	Diana B. Johannsen	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 October 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5* is/are pending in the application.

4a) Of the above claim(s) *1* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-5* is/are rejected.

7)☒ Claim(s) *4 and 5* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *3* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restriction

1. Applicant's election without traverse of Group II, claims 2-5, in Paper No. 10 is acknowledged.

2. Claim 1 is withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 10.

Information Disclosure Statement

3. Regarding the Form PTO 1449 provided with paper no. 3, it is noted that the examiner has corrected several typographical errors (in the citations for documents AG1, AN1, AW1, and AX1), and provided dates for two references (documents AD2 and AE2)(see the initialed and signed copy of Form PTO 1449 included herewith). It is requested that Applicants review and acknowledge the corrections made by the examiner.

Compliance with Sequence Rules

4. It is noted that the paper and computer readable forms of the Sequence Listing filed January 4, 2002 as part of paper no. 7 have been entered.

5. The specification contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR § 1.821(a) and (a)(2). However, the specification fails to comply with one or more of the requirements of 37 CFR § 1.821 through 1.825 because the specification recites sequences that lack description by the appropriate sequence identifier set forth in the

"Sequence Listing" as required by 37 CFR § 1.821(d). See, for example, pages 12 and pages 15-16, and Figures 6a-6b. Appropriate corrections for compliance are required.

Regarding Figures 6a-6b, it is noted that Applicant may either file substitute Figures that recite the appropriate sequence identifiers, or amend the brief description of the figures so as to set forth said sequence identifiers. See *MPEP* 2422.02.

Regarding the sequences set forth on pages 15-16, it is noted that sequences that constitute subsequences or fragments of SEQ ID NOs properly presented in the Sequence Listing may be identified by reference to the appropriate SEQ ID NO and the positions therein to which the subsequence or fragment corresponds (e.g., by amending the specification at the position immediately following the recited subsequence to recite "(nucleotides ___ to ___ of SEQ ID NO: ___)"). See *MPEP* 2422.03.

Specification

6. The use of the trademark DyNAzyme™ II has been noted in this application (see, e.g., p. 13). It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner that might adversely affect their validity as trademarks.

Claim Objections

7. Claims 4 and 5 are objected to because of the following informalities. In claim 4, there are two periods at the end of the claim. In claim 5, the names of several bacterial species are misspelled (specifically, *flavescens* is misspelled as "*flavescence*,"

intracellulare is misspelled as "*intraecllulare*," and *xenopi* is misspelled as "*xenopii*"). Claim 5 should also be amended such that a single space is provided between the genus and species designation in each species name, so as to conform with standard international nomenclature (e.g., by amending "*M.bovis*" to recite "*M. bovis*"). Appropriate correction is required.

8. It is also noted that the claims appear to be a literal translation into English from a foreign document, and include numerous grammatical and idiomatic errors. For example, claim 2 recites "diagnosis and identification Mycobacterium strain" rather than, e.g., "diagnosis and identification of a Mycobacterium strain," "comprising the step of" rather than "comprising the steps of," "one of the sequence" rather than "one of the sequences," "digesting...with restriction enzyme" rather than "digesting with a restriction enzyme," "isolating DNA fragment" rather than "isolating a DNA fragment," etc. The claims should be amended in a manner so as to correct such grammatical and idiomatic errors.

Claim Rejections - 35 USC § 112

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 2-5 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of identifying the species and/or subspecies of a mycobacterial strain in which the "DNA fragment" of claim 2, step b) corresponds to nucleotides 902-1261 of the *rpoB* gene of *M. tuberculosis* and/or to the

reference fragment of claim 2, step a), does not reasonably provide enablement for methods employing any "DNA fragment from microorganism to identify." The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." These factors include, but are not limited to: (A) the breadth of the claims; (B) the nature of the invention; (C) the state of the prior art; (D) the level of one of ordinary skill; (E) the level of predictability in the art; (F) the amount of direction provided by the inventor; (G) the existence of working examples; and (H) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) (*MPEP* 2164.01(a)).

The claims are drawn to methods of "diagnosis and identification Mycobacterium strain" comprising steps of "digesting a DNA fragment which has one of the sequence" of SEQ ID Nos 1-4 or 6-24 with a restriction enzyme to "obtain DNA fragment length polymorphism pattern," "isolating DNA fragment from microorganism to identify," "amplifying said DNA fragment," digesting "said amplified DNA fragment with the same restriction enzyme in step a)," "obtaining DNA fragment length polymorphism pattern from DNA fragment in step d)," and "comparing DNA fragment length polymorphism pattern from step a) with DNA fragment length polymorphism pattern from step e."

Claim 3 further requires that the fragment length polymorphisms of steps a) and e) be "obtained by electrophoresis." Claim 4 requires that "said restriction enzyme is characterized as" *Hae*III, *Msp*I, *Sau*3A1, or *Bst*EII. Claim 5 requires that "said Mycobacteria strain" be "characterized as" one of the mycobacterial species recited in the claim.

The specification discloses that Applicants' invention, in which a particular region of the *rpoB* gene is amplified and restriction digested, may be used to rapidly and accurately differentiate most mycobacterial species and some mycobacterial subspecies (see entire specification, particular, e.g., Figures 2 and 5, pages 6-9). Applicants exemplify their method and provide restriction fragment length patterns for numerous mycobacterial species (Figure 2, pages 10-14), and further provide an algorithm that may be employed in determining the species of, e.g., isolates of unknown species (see Figure 4). At pages 12-13, Applicants identify particular primers that may be employed in their method, and indicate that the region of the *rpoB* gene amplified and digested in their method corresponds to nucleotides 902-1261 of the *rpoB* gene of *M. tuberculosis*.

It is unpredictable as to whether one of skill in the art could use Applicants' invention in a manner reasonably commensurate with the instant claims. Given the guidance provided in the specification, one of skill in the art could clearly practice methods of determining the species and/or subspecies of a mycobacterial strain or isolate in which the particular DNA fragments, enzymes, and restriction digestions exemplified in the specification are employed (see pages 10-14 of the specification). It

is noted that the claims are sufficiently broad so as to encompass methods in which the particular enzymes and combinations of restriction digestions exemplified in the specification are not used. However, given the high level of skill of one of skill in the relevant art, it would not require undue experimentation to practice methods in which different enzymes are employed in the digestion of amplification products including the particular *rpoB* gene target region identified by Applicants. While the instant claims as written may encompass some inoperative embodiments, a skilled artisan could identify without undue experimentation those enzymes that could be employed successfully in methods requiring digestion of the target *rpoB* region identified by Applicants, and differentiate those enzymes from enzymes that would not be useful in such methods (see *MPEP* 2164.08(b) regarding inoperative subject matter). However, it is noted that the claims as written are not limited to methods in which the "DNA fragment" from the "microorganism to identify" (see step b) of claim 2) corresponds to or comprises the target *rpoB* gene region identified in the specification. While the claims do require the use of particular reference fragments that correspond to this region (one of SEQ ID NOS 1-4 or 6-24; see step a) of claim 2), the claims are sufficiently broad so as to encompass the isolation, amplification, and digestion of any DNA fragment from the "microorganism to identify." Thus the claims encompass the use of an extremely large genus of "DNA fragments" (specifically, any fragment obtained from a mycobacterial species). However, one of skill in the art would expect that only a small number of these fragments – specifically, those fragments corresponding to the target *rpoB* gene region disclosed in the specification (and corresponding to the reference DNA fragment

of step a) of claim 2) – could be employed in the method of the invention. The specification provides no guidance with respect to how one might use a DNA fragment lacking the critical *rpoB* region in the method of the invention. Lacking guidance from the specification, one of skill in the art may look to the teachings of the prior art for guidance and enablement of a claimed invention. However, while the prior art does disclose other methods in which PCR and RFLP are combined to identify mycobacterial species, the prior art methods require the use of corresponding test and reference DNA fragments (e.g., fragments prepared by amplification with the same set of primers), such that test patterns may be compared with a panel of reference patterns in order to achieve species identification. For example, Telenti et al (Journal of Clinical Microbiology 31(2):175-178 [2/1993]) disclose a PCR-RFLP method of differentiating mycobacterial species in which the same PCR-RFLP analysis is applied to test samples and to a panel of 40 reference strains; Talenti et al teach that the data from the analysis of the 40 reference strains was used to establish a diagnostic algorithm facilitating comparison of test sample patterns with reference patterns (see entire reference, particularly Figure 1). Further, it is well known to those of skill in the art that methods of PCR-RFLP require digestion of analogous fragments from test and reference samples in order for a meaningful comparison of restriction fragment patterns to be possible. Thus, both the teachings of the specification and the teachings of the prior art indicate that applicants method could not be practiced with any "DNA fragment," but would require the use of particular DNA fragments corresponding to the reference fragments of step a) in order to be useful and effective in differentiating mycobacterial species.

Further, given the teachings of the art with respect to the requirements for the successful use of PCR-RFLP (as exemplified, e.g., by Talenti et al), one of skill in the art would clearly recognize that no quantity of experimentation would allow one to practice a method of PCR-RFLP in which the test nucleic acid fragment employed in the method was not obtained by amplification of a sequence in the test sample corresponding to the reference sequence(s) employed in the method. Accordingly, while one of skill in the art could practice methods of identifying the species and/or subspecies of a mycobacterial strain in which the "DNA fragment" of claim 2, step b) corresponds to nucleotides 902-1261 of the *rpoB* gene of *M. tuberculosis* and/or to the reference fragment of claim 2, step a), it would require undue experimentation to use Applicants' invention in a manner reasonably commensurate with the instant claims.

11. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

12. Claims 2-5 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 2-5 are indefinite because it is unclear as to what must be accomplished in order to meet the requirements of the claimed method. First, it is unclear as to whether the claims are intended to be drawn to a method "of diagnosis and identification Mycobacterium strain," as set forth in the preamble of independent claim 2, or to a method of "comparing DNA fragment length polymorphism" patterns, as set forth in the final process step. Clarification is required with respect to how the comparing step f)

allows one to accomplish the "diagnosis and identification" set forth in the claim preamble. Further, the language "method of diagnosis and identification Mycobacterium strain" is vague and indefinite. The specification discloses a method that allows the species and/or subspecies of a mycobacterial isolate to be determined. However, the language of the claim does not make clear whether the claims are intended to be drawn to a method of determining the species of a particular strain or isolate, or whether the claims are intended to encompass methods of determining the particular mycobacterial strain of the "microorganism to identify" of claim 2, step b). Clarification is required.

Claims 2-5 are indefinite over the recitation of the phrase "isolating DNA fragment from microorganism to identify" in step b) of claim 2. It is unclear as to whether this phrase is intended to require one to isolate a DNA fragment from a microorganism that is to be identified by the claimed method (a "microorganism to identify"), or whether this language is intended to require one to isolate a DNA fragment from a microorganism 'to identify" that microorganism.

Claims 2-5 are indefinite over the recitation of the limitation "said DNA fragment" in claim 2, step c), because claim 2 previously refers to two different DNA fragments. It is unclear as to whether this recitation is intended to refer to the "DNA fragment" of step a) (the fragment subjected to "digesting") or to the "DNA fragment" of step b) (the fragment being isolated).

Claims 2-5 are indefinite over the limitation "said amplified DNA fragment" in claim 2, step d), because there is insufficient antecedent basis for this limitation in the claims. This rejection could be overcome by amending step c) of claim 2 to recite

"amplifying said DNA fragment of ____ (step a) or step b) – see rejection immediately above), thereby producing an amplified DNA fragment."

Claims 2-5 are indefinite over the recitation of the phrase "obtaining DNA fragment length polymorphism pattern from DNA fragment in step d)." It is unclear as to whether the recitation "DNA fragment in step d)" is intended to refer back to the "amplified DNA fragment" of step d), or whether this method step is intended to require, e.g., determining the pattern of the fragment(s) produced by digestion of the "amplified DNA fragment." Clarification is required.

Claims 3-4 are indefinite over the recitation of the phrase "wherein said DNA fragment length polymorphism from step a) and step e) are characterized as obtaining by electrophoresis" in claim 3. First, it is unclear as to whether the claim is intended to refer back to the "DNA fragment length polymorphism pattern" of step a) and step e), or to require, e.g., a type of "characterization" of the "DNA fragment length polymorphisms" of a) and e) by electrophoresis. Further, the recitation "are characterized as obtaining by electrophoresis" does not make clear whether the intent of claim 3 is to further limit one or more of the particular steps of claim 2 (e.g., to limit the manner in which the patterns of steps a) and e) or obtained), or to require an additional method step involving the characterization of "said DNA fragment length polymorphism from step a) and e)" in which electrophoresis is employed.

Claim 4 is indefinite over the recitation of the phrase "wherein said restriction enzyme is characterized as *HaeIII, MspI, Sau3A1 or BstEII*." It is unclear as to whether this language is intended to further limit the identity of the restriction enzyme employed

in the claimed method to one of those recited, whether this language is intended, e.g., to require the inclusion of additional steps of "characterizing" said restriction enzyme in some manner, to require describing/ "characterizing" the enzyme as one of those listed, etc.. This rejection could be overcome by amending the claim to recite, e.g., "wherein said restriction enzyme is *Hae*III, *Msp*I, *Sau*3A1 or *Bst*EII."

Claim 5 is indefinite over the recitation of the limitation "said Mycobacteria strain." There is insufficient antecedent basis for this limitation in the claims, as the claims previously recite a "Mycobacterium strain" but not a "Mycobacteria strain."

Claim 5 is indefinite over the recitation of the limitation "said Mycobacteria strain is characterized as..." First, it is unclear as to whether this recitation is intended to further limit the "Mycobacterium strain" of the claim preamble (such that the claim is limited to methods of identifying a particular strain/species), to further limit the "microorganism to identify" of step b) (such that the particular microorganism tested by the claimed method is determined to be one of those species recited in claim 5), to further limit the type of strain/species identified after the practice of method steps a)-f), etc. It is noted that the members of the group set forth in claim 5 are species, not particular strains. Clarification is required. Further, it is unclear as to whether the language "is characterized as" is intended to require additional method steps of "characterization" that result in the identification of the species of a strain, or whether this language is merely intended to limit the preamble, the "microorganism to identify," etc., as set forth above, or to otherwise further limit one of the previously recited steps of claim 2.

Claim Rejections - 35 USC § 102

13. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

14. Claims 2-5 are rejected under 35 U.S.C. 102(a) as being clearly anticipated by Lee et al (Journal of Clinical Microbiology 38(8):2966-2971 [8/2000]).

It is noted that the inventive entity of the instant invention is distinct from the authorship of the Lee et al reference and that this rejection may be overcome by the filing of a Katz-type declaration or by establishing priority of the invention to 10/27/1999 by filing a certified translation of priority document 1999-46795 (Republic of Korea).

The claims are drawn to methods of "diagnosis and identification Mycobacterium strain" comprising steps of "digesting a DNA fragment which has one of the sequences" of SEQ ID Nos 1-4 or 6-24 with a restriction enzyme to "obtain DNA fragment length polymorphism pattern," "isolating DNA fragment from microorganism to identify," "amplifying said DNA fragment," digesting "said amplified DNA fragment with the same restriction enzyme in step a)," "obtaining DNA fragment length polymorphism pattern from DNA fragment in step d)," and "comparing DNA fragment length polymorphism pattern from step a) with DNA fragment length polymorphism pattern from step e." Claim 3 further requires that the fragment length polymorphisms (FLP) of steps a) and e) be "obtained by electrophoresis." Claim 4 requires that "said restriction enzyme is characterized as" *Hae*III, *Msp*I, *Sau*3A1, or *Bst*EII. Claim 5 requires that "said

Mycobacteria strain" be "characterized as" one of the mycobacterial species recited in the claim.

Lee et al disclose a method of PCR-restriction fragment length polymorphism analysis (PRA) in which amplification and restriction digestion of a particular region of the *rpoB* gene is used to differentiate mycobacterial species (see entire reference).

Regarding step a) of the claimed method, in which a reference fragment of a particular sequence is digested, it is noted that in Lee et al's method, a particular region of the *rpoB* gene was amplified in each of a panel of mycobacterial reference strains, and the resulting amplification products were subjected to restriction digestion (see entire reference, particularly page 2966, right column and page 2967). The amplification products were analyzed by gel electrophoresis (Figure 1) and the patterns of restriction fragments observed were used to construct an algorithm for identification of mycobacterial species based on restriction fragment length polymorphism (RFLP)(see page 2968, left column, and Figure 2). It is noted that while Lee et al do not provide the sequences of the reference strain *rpoB* fragments amplified and digested in their method, the region of the *rpoB* gene amplified by Lee et al and the primers employed in that amplification are identical to those disclosed in the instant specification (see page 2967 of Lee, particularly the disclosure of the amplification of nucleotides 902-1261 with primers RPO5' and RPO3'; and the disclosure in the specification at pages 12-13 of the amplification of nucleotides 902-1261 with primers RPO5' and RPO3'). Further, the specific reference strains employed by Lee et al are identical to the reference strains employed by Applicants (compare Table 1 of Lee with Table 1 in

the specification, noting that all species/strains/sources are identical). As the *rpoB* gene sequence of a particular strain is an inherent property of that strain, and as Lee et al and Applicants amplified the same *rpoB* gene region with identical primers, it is an inherent property of the reference *rpoB* reference strain amplification products disclosed by Lee et al that they include each of instant SEQ ID Nos 1-4 and 6-24.

Regarding steps b)-f) of the claimed method, Lee et al disclose performing their PRA method on clinical isolates and employing their algorithm to determine the species thereof (see Figure 3 and page 2968, right column). The PRA method of Lee et al comprises steps of isolating genomic DNA from other cellular components, as required by step b) of the claimed method (see p. 2967, left column), amplification of a DNA fragment as in step c) (see p. 2967, left and right columns), digestion of the fragment with the same enzyme or enzymes employed in digestion of reference strain products (see p. 2967, right column, page 2968, right column, and Figures 1-3), and comparing fragment patterns with reference strain patterns using the algorithm of Figure 2 (see Figure 2 and page 2968, right column). Further, the method of Lee et al results in "diagnosis and identification" of the species of the tested strain/isolate (see Figure 3, and p. 2968, right column).

Regarding claims 3-4, Lee et al employ gel electrophoresis to obtain both test and reference RFLP patterns (see, e.g., Figures 1 and 3). With further regard to claim 4, Lee et al disclose the use in their methods of *Hae*III, *Msp*I, and *Sau*3A1 (see, e.g., p. 2967, right column, p. 2968, left column, and p. 2969, right column). Regarding claim 5, Lee et al disclose that their method may be employed in the differentiation of "most

mycobacterial species" (see p. 2968, left column, and Figure 2, which includes each of the species of claim 5), and exemplify the use of their method in determining the species of several mycobacterial strains (see, e.g., p. 2968, right column, and Figure 3, which exemplifies the identification of mycobacterial isolates as *M. intracellulare*, *M. gordonae*, and *M. abscessus*).

Accordingly, Lee et al clearly anticipate instant claims 2-5.

Conclusion

15. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. The prior art discloses methods of detecting and/or differentiating *Mycobacteria* in which nucleotide sequence differences are detected in regions of the *rpoB* gene differing from the region employed in Applicants' method. Specifically, Gingeras et al (U.S. Patent Application Publication 20002/0187467 A1 [12/2002; filed 4/1999]) disclose methods of classifying mycobacterial species by hybridization in which the probes employed hybridize to a target region of the *rpoB* gene upstream of Applicants' target region (see entire reference, especially page 3, paragraph 31, and Figure 1). Kook et al (U.S. Patent 6,242,584 B1 [6/2001; 102(e) date 3/1999) disclose a method of identifying mycobacterial species in which a portion of the *rpoB* gene located downstream of Applicants' target region is amplified and sequenced (see entire reference, especially column 4, lines 19-33).

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Diana B. Johannsen whose telephone number is

703/305-0761. The examiner can normally be reached on Monday-Friday, 7:30 am-4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones can be reached at 703/308-1152. The fax phone numbers for the organization where this application or proceeding is assigned are 703/872-9306 for regular communications and 703/872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703/308-0196.

Diana B. Johannsen
January 9, 2003